PATENT COOPERATION TREATY

PCT

REC'D 11 JUL 2005

WIPO PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference WOB03 IDM MYOG	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/EP2004/007891	International filing date *(day/month/year)* 15.07.2004	Priority date *(day/month/year)* 16.07.2003
International Patent Classification (IPC) or national classification and IPC A61K35/14, A61K35/34, C12N5/06, C12N5/08, A61P9/10, A61P9/04		
Applicant I.D.M. IMMUNO-DESIGNED MOLECULES et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14.12.2004	08.07.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Laffargue-Haak, T Telephone No. +49 89 2399-

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/007891

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-40	as originally filed
Claims, Numbers	
1-41	as originally filed
Drawings, Sheets	
1/19-19/19	as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/007891

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-19

because:

☒ the said international application, or the said claims Nos. 1-19 (IA only) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/007891

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	2-5, 8-10, 12-15, 17, 19, 21-26, 36-41
	No: Claims	1, 6, 7, 11, 11, 16, 18, 20, 27, 33-35
Inventive step (IS)	Yes: Claims	12, 21, 37
	No: Claims	1-11, 13-20, 22-32, 36, 38-41
Industrial applicability (IA)	Yes: Claims	1-19 : see separate sheet ; 20-41 YES
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

II. Priority

The priority is only partly valid. The feature "macrophage-conditioned medium" does not appear in the priority document. Consequently, claims 1-10 (partly), 12, 13-19 (partly) 21, 22-32 (partly), 37, 38-41 (partly) have an effective date of 15.07.2004 (i.e. filing date of the present application).

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 1-19 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability

Cited documents

Documents of the international search report ISR are numbered according to the order of appearance. Unless specified otherwise, reference is made to the passages cited in the ISR.

D1: WO 00/45827 A (BARTHOLEYNS JACQUES ; IDM IMMUNO DESIGNED MOLECULES (FR); KLEIN BERNAR) 10 August 2000.

D2: GHERARDI R K (REPRINT) ET AL: "Human myogenic precursor cells (mpc) attract monocytes through CC and CX3C chemokines and interplay with macrophages to improve muscle regeneration: A step toward characterization of the mpc niche" NEUROLOGY, (9 APR 2002) VOL. 58, NO. 7, SUPP. [3], PP. A45-A45, 9 April 2002 .

D3: CHAZAUD BENEDICTE ET AL: "Endoventricular porcine autologous myoblast transplantation can be successfully achieved with minor mechanical cell damage." CARDIOVASCULAR RESEARCH, vol. 58, no. 2, 1 May 2003, pages 444-450.

D4: ROBERTSON T A ET AL: "The role of macrophages in skeletal muscle regeneration with particular reference to chemotaxis" EXPERIMENTAL CELL RESEARCH, vol. 207, no. 2, 1993, pages 321-331.

D5: UTERO TRANSPLANTATION ET AL: "Myocyte and myogenic stem cell transplantation in the heart" CARDIOVASCULAR RESEARCH, (1 MAY 2003) VOL. 58, NO. 2, PP. 336-350.

D6: CHAZAUD, BENEDICTE ET AL: "Satellite cells attract monocytes and use macrophages as a support to escape apoptosis and enhance muscle growth" JOURNAL OF CELL BIOLOGY , 163(5), 1133-1143 2003.

Novelty

D1 discloses macrophages and stem cell based pharmaceutical compositions and the use thereof (see passages of the ISR) for cancer immunotherapy or stem cell transplantation. D1 is novelty destroying for

claims 1, 6, 7, 11, 16, 18, 20, 27 and 33-35.

Inventive step

Starting from D1 or D6 (for those claims not entitled to priority), the difference seems to reside in the use of a macrophage-conditioned medium. According to D4, macrophages and factors secreted by them are chemoattractants for muscle precursor cells. This does NOT hold for the so-called macrophage conditioned medium as such. Thus, the skilled person would not seriously consider the use of macrophage conditioned medium as an alternative to macrophages. The claims 1-41 thus involve an inventive step, *insofar the involve the use of macrophage conditioned medium.*

However, the use of macrophages in combination with myogenic stem cells is not considered inventive in view of D1 (closest prior art) and D2-D5, because it is already disclosed in the latter documents that macrophages improve the muscle regeneration if combined with myogenic precursor cells. The claims 1-41 thus do NOT involve an inventive step, *insofar the involve the use of macrophages.*

Industrial applicability

For the assessment of the present claims 1-19 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

VI. Certain documents cited

The document cited as P in the International Search Report is relevant, insofar the priority claim is not valid (see item II).

VIII. Certain observations on the international application

The claims as a whole are not concise, as there are three independent use claims, four independent product claims and two independent process claims (Art. 6 PCT).

The medical indication "a disease or a lesion involving cellular apoptosis, reduction of the survival of cells and/or destruction of cells" is not a clear definition of a disease to be treated (Art. 6 PCT).

It is unclear what is meant by "Binary complex" (claims 33-35) and this renders the scope of the claims

unclear (Art. 6 PCT).